IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: Weers et al. Application No: 10/616,448 Confirmation No: 1036 Filed: July 8, 2003 Title: PHOSPHOLIPID-BASED POWDERS FOR INHALATION	Group Art Unit: 1616 Examiner: Ernst V. Arnold Attorney Docket No: 53281-US-CNT[2] (NK.103.11) June 17, 2009 San Francisco, California 94107

APPEAL BRIEF

VIA ELECTRONIC FILING

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Examiner:

In response to the Examiner's Final Rejection of November 14, 2008 and the Notice of Appeal filed on February 17, 2009, the Applicant of the above-referenced patent application (hereinafter Appellant) hereby appeals to the Board of Patent Appeals and Interferences. Appellant requests the reversal of the Final Rejection.

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By: Melanie Hitchcock
Melanie Hitchcock

Date: June 17, 2009

(1) *Real Party in Interest*

The real party in interest of the present application is Novartis AG (by way of assignment from Novartis Pharmaceuticals AG and from Nektar Therapeutics, which was formerly Inhale Therapeutic Systems, Inc.), having a place of business at Forum 1, Novartis Campus, CH-4056 Basel, Switzerland.

(2) *Related Appeals and Interferences*

Appellant, Appellant's legal representative, and assignee are aware of no appeals or interferences which will directly affect or be directly affected by or have a bearing on the Board's decision in the present appeal.

(3) *Status of Claims*

Claims 1, 3-5, 11-15 and 21-34 are presently pending in the case. Claims 2, 6-10 and 16-20 have been cancelled. Claims 1, 3-5, 11-15 and 21-34 have been finally rejected. The rejection of each of claims 1, 3-5, 11-15 and 21-34 is hereby appealed.

(4) *Status of Amendments*

No amendments after Final Rejection have been filed. Accordingly, all amendments made during prosecution of the case have been entered.

(5) *Summary of the Claimed Subject Matter*

As recited in claim 1, a method is provided for the pulmonary administration of a dry powder composition from a passive dry powder inhaler to the respiratory tract of a patient (see page 7 through page 18). The method comprises providing a dry powder composition comprising particles comprising a lipid matrix and an active agent, and the particles having a particle size of 1-30 microns, mass median aerodynamic diameter of

less than 5 microns, and bulk density of less than 0.5 g/cm^3 (see page 11 line 21 through page 12 line 14). The method further comprises loading the dry powder composition into a passive dry powder inhaler (see page 6 lines 18-22) having a resistance of from 0.01 to 0.30 $(cmH_20)^{1/2}/Lmin^{-1}$ (see page 7 lines 17-25). The dry powder is administered from the inhaler to the respiratory tract of a patient, wherein the emitted dose is at least 60% for flow rates from 10 to 60 liters per minute (see page 7 lines 21-25).

As recited in claim 21, a method is provided for the pulmonary administration of a dry powder composition from a passive dry powder inhaler to the respiratory tract of a patient (see page 7 through page 18). The method comprises providing a dry powder composition comprising particles comprising a lipid matrix and an active agent, and the particles having a particle size of 1-30 microns, mass median aerodynamic diameter of less than 5 microns, and bulk density of less than 0.5 g/cm^3 (see page 11 line 21 through page 12 line 14). The method further comprises loading the dry powder composition into a passive dry powder inhaler (see page 6 lines 18-22) having a resistance of from 0.01 to 0.30 $(cmH_20)^{1/2}/Lmin^{-1}$ (see page 7 lines 17-25). The dry powder is administered from the inhaler to the respiratory tract of a patient, wherein the fine particle fraction emitted from the inhaler is at least 60% as determined by an Anderson Cascade Impaction or multi-stage liquid impinger (see page 7 lines 21-25 and Example 4).

As recited in claim 29, a method is provided for the pulmonary administration of a dry powder composition from a passive dry powder inhaler to the respiratory tract of a patient (see page 7 through page 18). The method comprises providing a dry powder composition comprising particles comprising: (i) a lipid matrix comprising a phospholipid selected from the group consisting of dipalmitoylphosphatidylcholine, distearoylphosphatidylcholine, diarachidoylphosphatidycholine, dibehenoylphosphatidylcholine, diphosphatidyl glycerol, phosphatidylcholines, saturated phosphatidylethanolamines, saturated phosphatidylserines, saturated phosphatidylglycerols, and saturated phosphatidylinositols (see pages 8 and 9); (ii) an

active agent comprising tobramycin sulfate (see Example 5); (iii) a particle size of 1-30 microns; (iv) a mass median aerodynamic diameter of less than 5 microns; and (v) a bulk density of less than 0.5 g/cm^3 (see page 11 line 21 through page 12 line 14). The method further comprises loading the dry powder composition into a passive dry powder inhaler (see page 6 lines 18-22) having a resistance of from 0.01 to 0.30 $(cmH_20)^{1/2}/Lmin^{-1}$ (see page 7 lines 17-25). The dry powder is administered from the inhaler to the respiratory tract of a patient, wherein the fine particle fraction emitted from the inhaler is at least 60% as determined by an Anderson Cascade Impaction or multi-stage liquid impinger (see page 7 lines 21-25 and throughout the specification).

(6) *Grounds of Rejection to be Reviewed on Appeal*

Appellant requests review of the Examiner's following grounds of rejection:

Claims 1, 3-5, 11-15 and 21-34 have been rejected under 35 U.S.C. §103(a) as being unpatentable over U.S. Patent No. 6,116,237 to Schultz et al (hereinafter Schultz et al) in view of U.S. Patent No. 5,855,913 to Hanes et al (hereinafter Hanes et al) and U.S. Patent No. 5,049,389 to Radhakrishnan (hereinafter Radhakrishnan).

Claims 1, 3-5, 11-15 and 21-34 have been rejected under the judicially created doctrine of double patenting as being unpatentable over the claims of U.S. Patent Application No. 09/851,226 (now US Patent 7,442,388) in view of Schultz et al and Hanes et al.

Claims 1, 3-5, 11-15 and 21-34 have been rejected under the judicially created doctrine of double patenting as being unpatentable over the claims of U.S. Patent Application No. 10/141,219 in view of Schultz et al.

Claims 1, 3-5, 11-15 and 21-34 have been rejected under the judicially created doctrine of double patenting as being unpatentable over the claims of U.S. Patent Application No. 11/187,757 in view of Schultz et al.

Claims 1, 3-5, 11-15 and 21-34 have been rejected under the judicially created doctrine of double patenting as being unpatentable over the claims of U.S. Patent 7,306,787 in view of Schultz et al.

(7) *Argument*

Appellant believes each of claims 1, 3-5, 11-15 and 21-34 are improperly rejected and are therefore allowable for the following reasons.

The rejection of independent claim 1 under 35 U.S.C. §103(a) is improper

The rejection of independent claim 1 under 35 U.S.C. §103(a) is improper because the Examiner has failed to establish a prima facie case in that the Examiner has not accounted for all limitations in the claim. "All words in a claim must be considered in judging the patentability of that claim against the prior art." In re Wilson, 424 F.2d 1382, 1385. When a prima facie case is not established by the Examiner, the Examiner has not satisfied his or her burden and Applicant is under no obligation to provide evidence in rebuttal of the alleged obviousness. In re Rinehart, 531 F.2d 1048; In re Linter, 458 F.2d 1013; In re Saunders, 444 F.2d 599; In re Tiffin, 443 F.2d 394, *amended*, 448 F.2d 791; In re Warner, 379 F.2d 1011, *cert. denied*, 389 U.S. 1057 (1968).

The Examiner has failed to properly consider and account for all limitations in claim 1. Claim 1 is to a method comprising, inter alia, loading a dry powder composition into a passive dry powder inhaler. Schultz et al, the primary reference relied upon by the Examiner, does not disclose a passive dry powder inhaler. Instead, Schultz et al discloses an active dry powder inhaler.

As known in the art, dry powder inhalers are classified as either active dry powder inhalers or passive dry powder inhalers. As defined by the Appellant in on page 6 lines 18-22 of the specification and as known in the art, a "passive dry powder inhaler" refers to an inhalation device which relies on the patient's inspiratory effort to disperse and aerosolize a drug formulation. As further explained, a "passive dry powder inhaler" does not include inhaler devices which comprise a means for providing energy to disperse and aerosolize the drug formulation. In contrast to that which Applicant claims, Schultz et al discloses an active dry powder inhaler that relies on a motor and impeller (see column 4 lines 49-57 and column 6 lines 32-58) to at least assist in the aerosolization and/or delivery of the dry powder to a user. Thus, the primary reference Schultz et al does not disclose or suggest a passive dry powder inhaler.

The secondary references relied on by the Examiner offer no salvo to the Examiner's failure to account for the passive dry powder inhaler limitation in claim 1. Hanes et al and Radhakrishnan are not relied on to teach the use of a passive inhaler, nor do they. Accordingly, the combination of references proffered by the Examiner as obvious does not meet all limitations recited in claim 1.

Furthermore, the Examiner makes no attempt to posit that it would have been obvious to one of ordinary skill in the art to substitute a passive dry powder inhaler for Schultz et al's active dry powder inhaler. Instead, the Examiner contends that the Schultz et al device is a passive dry powder inhaler because the user has to inhale in order to deliver the powder to the lungs (see Final Office action pages 7 and 8). However, such user inhalation does not render a device as passive. Verily, most (if not all) active dry powder inhalers utilize a patient's inhalation to deliver aerosolized powder to the lungs. On the other hand, no passive dry powder inhalers use means for providing energy to disperse and aerosolize the drug formulation, as Schultz et al's device does. The Examiner then goes on to nonsensically conclude that Schultz et al teaches a passive dry powder inhaler because Schultz et al's claims are broad enough to encompass passive dry powder inhalers. However, this contention holds no water as the scope of Schultz et al's claims has no relevance in the present situation to what

Schultz et al teaches one of ordinary skill in the art. To the contrary, one of ordinary skill in the art would clearly find the teachings of Schultz et al to be of an active dry powder inhaler.

Thus, the Examiner has not shown a passive dry powder inhaler in the primary reference or as an obvious modification. Accordingly, the Examiner has not adequately considered and accounted for all limitations in claim 1, and the Examiner has failed to establish a prima facie case under 35 U.S.C. §103(a).

Since a prima facie case has not been established, the Examiner has not met his burden, and Appellant's argument can adequately end here. However, for the sake of completeness, Appellant further points out that it would have not have been obvious to one having ordinary skill in the art at the time the invention was made to modify Schultz et al in a manner that would arrive at Appellant's invention as set forth in claim 1. First, there is no motivation provided by either the references or by the Examiner to modify Schultz et al from an active to a passive device. Secondly, one of ordinary skill in the art would not have found it obvious to modify Schultz et al from an active to a passive device because doing so would go expressly against the teachings of Schultz et al. As discussed throughout Schultz et al, the motor and impellar system is designed to make the Schultz et al device flow rate independent (see abstract, column 3 lines 32-40, and column 4 lines 1-2). Thus, a modification to make the active inhaler of Schultz et al into a passive inhaler would fly in the face of the teachings of Schultz et al and would not have been obvious to one having ordinary skill in the art, particularly in the absence of any motivation to do so.

For at least these reasons, claim 1 is not properly rejectable under 35 U.S.C. §103(a) as being unpatentable over Schultz et al, Hanes et al and Radhakrishnan. Appellant requests reversal of the rejection of claim 1 under 35 U.S.C. §103(a). In addition, Appellant requests reversal of the rejection of claims 3-5 and 11-15, which depend from claim 1 and are not rendered unpatentable by Schultz et al, Hanes et al and Radhakrishnan for at least the same reasons as claim 1.

The rejection of independent claim 21 under 35 U.S.C. §103(a) is improper

In addition, independent claim 21 is not rendered unpatentable by Schultz et al, Hanes et al and Radhakrishnan. Claim 21 is to a method comprising, inter alia, loading a dry powder composition into a passive dry powder inhaler. Schultz et al does not disclose or suggest a passive dry powder inhaler, as discussed above. Furthermore, Hanes et al and Radhakrishnan do not make up for the deficiency. Accordingly, there is no prima facie case of obviousness under 35 U.S.C. §103(a) established against claim 21. Moreover, it would not have been obvious to modify Schultz et al in that (i) there is not motivation to make the modification and (ii) Schultz et al teaches away from any such modification.

For at least these reasons, claim 21 is not properly rejectable under 35 U.S.C. §103(a) as being unpatentable over Schultz et al, Hanes et al and Radhakrishnan. The modification that would be necessary is not one that would have been well within the grasp of one of ordinary skill in the art at the time the invention was made. There is no evidence to suggest that this is a situation where the ordinary artisan could have been motivated to modify Schultz et al in a manner that would result in the invention of claim 21 and there is no evidence to suggest the artisan would have seen the benefit in doing so. Thus, claim 21 is allowable over the references cited.

Appellant requests reversal of the rejection of claim 21 under 35 U.S.C. §103(a). In addition, Appellant requests reversal of the rejection of claims 22-28 that depend from claim 21 and are not rendered unpatentable by Schultz et al, Hanes et al and Radhakrishnan for at least the same reasons as claim 21.

The rejection of independent claim 29 under 35 U.S.C. §103(a) is improper

Independent claim 29 is not rendered unpatentable by Schultz et al, Hanes et al and Radhakrishnan, either. Claim 29 is to a method comprising, inter alia, loading a dry

powder composition into a passive dry powder inhaler. Schultz et al does not disclose or suggest a passive dry powder inhaler, as discussed above. Furthermore, Hanes et al and Radhakrishnan do not make up for the deficiency. Accordingly, there is no prima facie case of obviousness under 35 U.S.C. §103(a) established against claim 29. Moreover, it would not have been obvious to modify Schultz et al in that (i) there is not motivation to make the modification and (ii) Schultz et al teaches away from any such modification.

For at least these reasons, claim 29 is not properly rejectable under 35 U.S.C. §103(a) as being unpatentable over Schultz et al, Hanes et al and Radhakrishnan. The modification that would be necessary is not one that would have been well within the grasp of one of ordinary skill in the art at the time the invention was made. There is no evidence to suggest that this is a situation where the ordinary artisan could have been motivated to modify Schultz et al in a manner that would result in the invention of claim 29 and there is no evidence to suggest the artisan would have seen the benefit in doing so. Thus, claim 29 is allowable over the references cited.

Appellant requests reversal of the rejection of claim 29 under 35 U.S.C. §103(a). In addition, Appellant requests reversal of the rejection of claims 30-34 which depend from claim 29 and are not rendered unpatentable by Schultz et al, Hanes et al and Radhakrishnan for at least the same reasons as claim 29.

Claims are not properly rejected under judicially created doctrine of Double Patenting

The Examiner improperly provisionally rejected claims 1, 3-5, 11-15 and 21-34 under the judicially created doctrine of double patenting as being unpatentable over the claims of U.S. Patent Application No. 09/851,226 (now US Patent 7,442,388) in view of Schultz et al and Hanes et al.

The Examiner has failed to establish a proper rejection under the judicially created doctrine of Double Patenting. The claims of 7,442,388 do not recite a passive

dry powder inhaler of the type recited in Appellant's present independent claims. Schultz et al and Hanes et al do not teach a passive dry powder inhaler of the type claimed. Thus, the references are not combinable with the claims of 7,422,388 in a manner that would render Appellant's claims as properly rejectable under the judicially created doctrine of double patenting. Thus, Applicant requests reversal of the provisional double patenting rejection.

The Examiner also improperly provisionally rejected claims 1, 3-5, 11-15 and 21-34 under the judicially created doctrine of double patenting as being unpatentable over the claims of U.S. Patent Application No. 10/141,219 in view of Schultz et al.

The Examiner has again failed to establish a proper rejection under the judicially created doctrine of Double Patenting. The claims of 10/141,219 do not recite a passive dry powder inhaler of the type recited in Appellant's present independent claims. Schultz et al and Hanes et al do not teach a passive dry powder inhaler of the type claimed. Thus, the references are not combinable with the claims of 10/141,219 in a manner that would render Appellant's claims as properly rejectable under the judicially created doctrine of double patenting. Thus, Applicant requests reversal of the provisional double patenting rejection.

The Examiner yet again improperly provisionally rejected claims 1, 3-5, 11-15 and 21-34 under the judicially created doctrine of double patenting as being unpatentable over the claims of U.S. Patent Application No. 11/187,757 in view of Schultz et al.

The Examiner has failed to establish a proper rejection under the judicially created doctrine of Double Patenting. The claims of 11/187,757 do not recite a passive dry powder inhaler of the type recited in Appellant's present independent claims. Schultz et al and Hanes et al do not teach a passive dry powder inhaler of the type claimed. Thus, the references are not combinable with the claims of 11/187,757 in a manner that would render Appellant's claims as properly rejectable under the judicially

created doctrine of double patenting. Thus, Applicant requests reversal of the provisional double patenting rejection.

Finally, the Examiner improperly rejected claims 1, 3-5, 11-15 and 21-34 under the judicially created doctrine of double patenting as being unpatentable over the claims of U.S. Patent 7,306,787 in view of Schultz et al.

The Examiner has failed to establish a proper rejection under the judicially created doctrine of Double Patenting. The claims of 7,306,787 do not recite a passive dry powder inhaler of the type recited in Appellant's present independent claims. Schultz et al and Hanes et al do not teach a passive dry powder inhaler of the type claimed. Thus, the references are not combinable with the claims of 7,306,787 in a manner that would render Appellant's claims as properly rejectable under the judicially created doctrine of double patenting. Thus, Applicant requests reversal of the double patenting rejection.

Conclusion

Thus, it is believed that all rejections made by the Examiner have been addressed and overcome by the above arguments. Therefore, all pending claims are allowable. A reversal is respectfully requested.

Should there be any questions, Appellant's representative may be reached at the number listed below.

Respectfully submitted,

JANAH & ASSOCIATES

Dated: June 17, 2009

By: _____
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(8) Claims Appendix

1. A method for the pulmonary administration of a dry powder composition from a passive dry powder inhaler to the respiratory tract of a patient, the method comprising:

providing a dry powder composition comprising particles comprising a lipid matrix and an active agent, and the particles having a particle size of 1-30 microns, mass median aerodynamic diameter of less than 5 microns, and bulk density of less than 0.5 g/cm^3;

loading the dry powder composition into a passive dry powder inhaler having a resistance of from 0.01 to 0.30 $(cmH_20)^{1/2}/Lmin^{-1}$; and

administering the dry powder composition from the inhaler to the respiratory tract of a patient,

wherein the emitted dose is at least 60% for flow rates from 10 to 60 liters per minute.

3. A method according to claim 1 wherein the emitted dose is at least 80% for flow rates from 10 to 60 liters per minute.

4. A method according to claim 1 wherein the fine particle fraction, which is the fraction of the particles emitted from the inhaler as determined by an Anderson Cascade Impaction or multi-stage liquid impinger, is at least 60%.

5. A method according to claim 1 wherein the lipid comprises a phospholipid selected from the group consisting of dipalmitoylphosphatidylcholine, distearoylphosphatidylcholine, diarachidoylphosphatidycholine, dibehenoylphosphatidylcholine, diphosphatidyl glycerol, phosphatidylcholines, saturated phosphatidylethanolamines, saturated phosphatidylserines, saturated phosphatidylglycerols, and saturated phosphatidylinositols.

11. A method according to claim 1 wherein the lung deposition is greater than 25%.

12. A method according to claim 1 wherein the lung deposition is greater than 30%.

13. A method according to claim 1 wherein the lung deposition is greater than 50%.

14. A method according to claim 1 wherein the active agent is selected from the group consisting of budesonide, tobramycin sulfate, leuprolide acetate, amphotericin B and parathyroid hormone.

15. A method according to claim 1 wherein the particles comprise hollow porous microparticles.

21. A method for the pulmonary administration of a dry powder composition from a passive dry powder inhaler to the respiratory tract of a patient, the method comprising:

providing a dry powder composition comprising particles comprising a lipid matrix and an active agent, and the particles having a particle size of 1-30 microns, mass median aerodynamic diameter of less than 5 microns, and bulk density of less than 0.5 g/cm^3;

loading the dry powder composition into a passive dry powder inhaler having a resistance of from 0.01 to 0.30 $(cmH_20)^{1/2}/Lmin^{-1}$; and

administering the dry powder composition from the inhaler to the respiratory tract of a patient,

wherein the fine particle fraction emitted from the inhaler is at least 60% as determined by an Anderson Cascade Impaction or multi-stage liquid impinger.

22. A method according to claim 21 wherein the emitted dose is at least 60% for flow rates from 10 to 60 liters per minute.

23. A method according to claim 22 wherein the emitted dose is at least 80% for flow rates from 10 to 60 liters per minute.

24. A method according to claim 21 wherein the lipid comprises a phospholipid selected from the group consisting of dipalmitoylphosphatidylcholine, distearoylphosphatidylcholine, diarachidoylphosphatidycholine, dibehenoylphosphatidylcholine, diphosphatidyl glycerol, phosphatidylcholines, saturated phosphatidylethanolamines, saturated phosphatidylserines, saturated phosphatidylglycerols, and saturated phosphatidylinositols.

25. A method according to claim 21 wherein the lung deposition is greater than 25%.

26. A method according to claim 25 wherein the lung deposition is greater than 50%.

27. A method according to claim 21 wherein the active agent is selected from the group consisting of budesonide, tobramycin sulfate, leuprolide acetate amphotericin B and parathyroid hormone.

28. A method according to claim 21 wherein the particles comprise hollow porous microparticles.

29. A method for the pulmonary administration of a dry powder composition from a passive dry powder inhaler to the respiratory tract of a patient, the method comprising:

providing a dry powder composition comprising particles comprising:

(i) a lipid matrix comprising a phospholipid selected from the group consisting of dipalmitoylphosphatidylcholine, distearoylphosphatidylcholine, diarachidoylphosphatidycholine, dibehenoylphosphatidylcholine, diphosphatidyl glycerol, phosphatidylcholines, saturated phosphatidylethanolamines, saturated phosphatidylserines, saturated phosphatidylglycerols, and saturated phosphatidylinositols;

(ii) an active agent comprising tobramycin sulfate;

(iii) a particle size of 1-30 microns;

(iv) a mass median aerodynamic diameter of less than 5 microns; and

(v) a bulk density of less than 0.5 g/cm^3;

loading the dry powder composition into a passive dry powder inhaler having a resistance of from 0.01 to 0.30 $(cmH_20)^{1/2}/Lmin^{-1}$; and

administering the dry powder composition from the inhaler to the respiratory tract of a patient,

wherein the fine particle fraction emitted from the inhaler is at least 60% as determined by an Anderson Cascade Impaction or multi-stage liquid impinger.

30. A method according to claim 29 wherein the emitted dose is at least 60% for flow rates from 10 to 60 liters per minute.

31. A method according to claim 30 wherein the emitted dose is at least 80% for flow rates from 10 to 60 liters per minute.

32. A method according to claim 29 wherein the lung deposition is greater than 25%.

33. A method according to claim 32 wherein the lung deposition is greater than 50%.

34. A method according to claim 29 wherein the particles comprise hollow porous microparticles.

(9) Evidence Appendix

none

(10) Related Proceedings Appendix

none